REMARKS

I. Status of the Claims

Claims 9, 15 and 17 are amended.

Claims 10, 13, 16 are cancelled.

Claims 1-8 are withdrawn (note that original, withdrawn claim 6 was inadvertently omitted in the amendment mailed June 28, 2006, and the error was perpetuated without notice because it was withdrawn. Claim 6 is included herein).

Claims 9, 11-12, 14-15 and 17 are being prosecuted.

II. Claims 13, 16 and 17 Comply with 35 U.S.C. §112

Applicant thanks the Examiner for recognizing that claim 11 and a 2.5 – 10 mg daily dose range of doxepin complies with 35 U.S.C. §112. The Examiner admits that standard doses of non-narcotic analgesics range from 0.5-2.6 gram daily (Claim 17; Office Action, p. 3).

However, the Examiner does not accept that the unit doses of claims 13, 16, and 17 have support in the specification. Although applicant disagrees, to advance the prosecution, claims 13 and 16 have been cancelled.

By this amendment, claim 17 has been modified to recite a daily dose range 0.5 – 2.6 gm, of non-narcotic analgesics as the Examiner agrees is supported in the specification (Office Action, p. 3).

Therefore, Applicant respectfully submits that the rejection of claim 17 under 35 USC Sec. 112, first paragraph has been overcome.

III. Caruso Does Not Anticipate Because Caruso Does Not Teach All Claim Elements

Claim 9-15, 17 were rejected under 35 USC Sec. 102(b) as allegedly anticipated by Caruso (WO 98/50044). Applicant respectfully traverses the rejection.

By this amendment, claims 9, 11, 15 and 17 have been amended, and claims 10 and 13 have been cancelled.

In claim 9, applicant agrees that "consisting essentially of" should include materials specified in the claim "and those that do not materially affect the basic and novel characteristics of the claimed invention." (see MPEP 2111.03) As explained in the record, applicant believes this term "excludes NMDA receptor blockers of Caruso."

The Examiner requested a showing of enhanced or improved results over Caruso. The improvement is the lower tricyclic antidepressant doses claimed herein which have eliminated side effects, notably sedation and anticholinergic side effects such as dry mouth, blurred vision and urinary retention. Furthermore, there is no law presented to support this request to overcome anticipation.

Caruso teaches only an antidepressant, the invention presented to those of skill in the art is

> effectiveness of an antidepressant is significantly potentiated by administering the antidepressant prior to, with or following the administration of a nontoxic NMDA receptor antagonist.

for alleviation of "neuropathic pain." (Caruso, Abstract and p. 1). To alleviate this level of pain, much higher doses than claimed herein, are necessary.

Unless "a nontoxic NMDA receptor antagonist" as defined on p.1, lines 19-24, is the same as a "non-narcotic analgesic" in present claim 9, Caruso does not anticipate because it does not have all claimed elements. Examples of non-narcotic analgesics in the present application are acetaminophen and NSAIDs (e.g., aspirin, ibuprofen, flurbiprofen, ketoprofen, and naproxen). Furthermore, Caruso's contribution to an obviousness rejection is at most providing an "antidepressant."

It would be clear to those of skill in the art that what Caruso **teaches is** a composition of

- antidepressant plus
- non-toxic NMDA receptor antagonist.

The entire thrust of the invention is these two components, as set forth in claim 9 as amended. The teaching is that in combination they improve pain relief. The entire Summary, and the first three pages of the Description of the Preferred Embodiments must be read until page 7, lines 10-24 referred to by the Examiner, in which a laundry list of "optionally" included "pharmacologically active substances" appears – over 50 (fifty) of such substances are listed. In the laundry list there is a category "non-narcotic analgesics" – the second component of the two part composition of the present claims, but there is no guidance to select one of the multiple optional categories, nor any discussion of what they would add to the effects of Caruso's invention that would teach one of skill in the art to make a composition **including** an **optional** component of Caruso's composition and **excluding** an **essential** compound.

Doses (325 mg) of some non-narcotic analgesics are only provided for these optional ingredients within a table format called "Examples 1-46". These must be in combination with not

only an antidepressant, but also a non-toxic NMDA receptor antagonist. This is not teaching the present claims. One of skill in the art would not be led to tease out of a laundry list, the combination presently claimed. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species).

The Examiner asserts that "intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art," citing *Casey* and *Otto*. There **is** a "structural difference" – all Caruso's compositions have a "non-toxic NMDA receptor antagonist" which the present claimed compositions **do not have**. In *Ex Parte Hervy A. Morris*, 1998 WL 1736155 (BPAI) *Otto* and *Casey* are referred to as stating that "a method concept ... may not be relied on to distinguish a structural claim over the prior art," but "a structural limitation that is necessarily present to function." If that structural limitation is not present, there is no anticipation. The Board also notes "[t]here is nothing intrinsically wrong in defining something by what it does rather than by what it is," citing *In re Echerd*, 176 USPQ 321, 322 (CCPA 1973).

In order to anticipate a claimed invention, a prior art reference must enable one of ordinary skill in the art to make the invention without undue experimentation. *FinisarCorp. v. DirecTV Group, Inc.*, 523 F.3d 1323, 1336 (Fed. Cir. 2008) (citing *In re Omeprazole Patent Litig.*, 483 F.3d 1364, 1379 (Fed. Cir. 2007). In other words, the prior art must enable the claimed invention. *Minn. Mining & Mfg. Co. v. Chemque, Inc.(3M)*, 303 F.3d 1294, 1301 (Fed. Cir. 2002).

There is simply no description of a composition of a very low dose of doxepin with a non-narcotic analgesic as set forth in claim 9 as amended in the cited art of Caruso. Claims 11, 12, 14, 15 and 17 are more specific dependent claims. Therefore, there is also no anticipation of the related dependent claims in the cited art.

Applicant respectfully requests that the rejection under 35 USC Sec. 102(b) over Caruso be withdrawn.

IV. Kakuyama *et al.* Is Not Enabling

Claims 9-11, 13-14 and 17 are rejected as anticipated by Kakuyama have been rejected under 35 USC Sec. 102(b) as allegedly anticipated by Kakuyama *et al.* (*Pain Reviews* 2000; 7: 119-128). Applicant respectfully traverses the rejection.

By this amendment, claims 10 and 13 have been cancelled, and claims 9, 11 and 17 have been modified. Claim 14 depends on modified claim 9.

Applicant respectfully continues to assert that Kakuyama *et al.* does not anticipate independent claim 9; as it is not enabling prior art, because the reference provides no structure, no doses nor specific compositions. The more specific dependent claims 11, 14 and 17 are also not anticipated by the cited art.

The focus of Kakuyama and Fukuda, as evidenced by the title and all but one (1) paragraph of an 8 page paper is "The role of **antidepressants** ..." – only one of the presently claimed components. This is a review, not a scientific report, and includes MEDLINE searches. 57 reports are summarized.

The paragraph on which the Examiner bases her rejection (page 125, right hand column fourth full paragraph) includes among many summaries, a reference to Goldenberg *et al.*, who included "an NSAID, naproxen 1000 mg/day and amitriptyline 25 mg every night." These are **not** one composition as in the present claims but rather two drugs taken; one in the day, one at night. The groups including amitriptyline showed "significant improvement" but no details are provided to suggest the combination was better than amitriptyline alone, so one of skill would not have been lead to treat chronic pain with a combination based on the teachings of Kakuyama *et al.* or Caruso either singly or in combination. The Examiner ignores that crucial explanation. The Examiner does not admit that the combination was only as effective as the antidepressant alone, which illustrates the surprising results of the invention as set forth in independent claim 9 as amended. Why would those of skill in the art give two drugs, when one was sufficient? That would increase risk of side effects.

There is simply no description of a composition of a very low dose of doxepin with a non-narcotic analgesic as set forth in claim 9 as amended in the cited art of Kakuyama *et al.* Claims 11, 14 and 17 are more specific dependent claims. Therefore, there is also no anticipation of the related dependent claims in the cited art.

Applicant respectfully requests that the rejection under 35 USC Sec. 102(b) over Kakuyama *et al.* be withdrawn.

V. A *Prima Facie* Case of Obviousness is light of Kakuyama *et al.* and Caruso is Not Established

Claims 12 and 15 have been rejected under 35 USC Sec. 103(a) as alledgely obvious over the combined teachings of Kakuyama et al. (*Pain Reviews* 2000; 7: 119-128) and Caruso (WO 98/50044). Applicant respectfully traverses the rejection.

For the sake of brevity, the arguments in section IV and V above concerning Caruso and Kakuyama *et al.* are incorporated by reference herein. A *prima facie* case of obviousness is not established because all the claimed elements are not in the combination.

There is simply no teaching or suggestion of the composition of a very low dose of doxepin with a non-narcotic analgesic, further defined by salts as set forth in claim 12 or in specific vehibles as set forth in claim 15 as amended, in the combined teaching of the cited art of Kakuyama *et al.* and Caruso. Applicant respectfully requests that the rejection under 35 USC Sec. 103(a) over Kakuyama *et al.* and Caruso be withdrawn.

VI. A *Prima Facie* Case of Obviousness is light of Crawford *et al.* and Lombardino is Not Established

Claims 9-17 have been rejected under 35 USC Sec. 103(a) as allegedly obvious over the combined teachings of Crawford et al. (U.S. Patent No. 4,579,846) and Lombardino (U.S. Patent No. 4,434,164). Applicant respectfully traverses the rejection.

Claims 9, 11, 15 and 17 have been amended and claims 10, 13 and 16 have been cancelled by this amendment.

The Examiner admits that Crawford *et al.* teaches piroxicom with doxepin, although separately administered and that "Crawford *et al.* does not specifically teach that the compositions as exemplified comprise 'a standard dose'...and a low dose..." in the present Office Action at p. 16.

Lombardino is cited to supply a "standard dose" of piroxicom.

The Examiner's arguments, mixing and matching parts of these two publications guided by hindsight, are insufficient to establish a *prima facie* case of obviousness over independent claim 9 as amended.

The arguments against the citation of *In re Casey* and *In re Otto* from Section III herein are incorporated by reference.

A determination of obviousness requires that "the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved." *KSR International Co. v. Teleflex, Inc.*, -- U.S. --, 127 S.Ct. 1727, 1734, 82 U.S.P.Q.2d 1385 (2007) *quoting Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). In making a determination of obviousness by looking at the teachings of multiple patents, one should consider

> the effects of demands known to the design community or present in the market place; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. *To facilitate review, this analysis should be made explicit.*

KSR, 127 S.Ct. at 1740-41 *(emphasis added)*. "[A] patent composed of several elements is not proved obvious merely by demonstrating the each of its elements was, independently, known in the prior art." *Id.* at 1741.

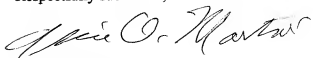
There is simply no teaching or suggestion of the composition of a very low dose of doxepin with a non-narcotic analgesic as set forth in claim 9 as amended, in the combined teachings of the cited art of Crawford et al. and Lombardino. Claims 11, 12, 14, 15 and 17 depend from claim 9. Applicant respectfully submits that the more specific dependent claims are also patentable over the combined teachings of the cited art for the same reason that claim 9 is free of the cited art.

Applicant respectfully requests that the rejection under 35 USC Sec. 103(a) over Crawford et al. and Lombardino be withdrawn.

VII. Conclusions

For the reasons stated herein, Applicant respectfully requests that the outstanding rejections be withdrawn and that all of the pending claims be allowed. No other fees are believed due at this time, however, please charge any additional deficiencies or credit any overpayments to deposit account number 12-0913 with reference to our attorney docket number (41957-102748).

Respectfully submitted,



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